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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/684,599	10/05/2000	Ira Pastan	15280-259120US	2466

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EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/684,599	PASTAN ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *12/7/05, 3/2/06*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *19-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *19-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 11500
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Amendments filed December 7, 2005 and March 2, 2006 in response to the Office Action of June 3, 2005 and the telephone interview of February 28, 2006 are acknowledged and have been entered. Previously pending claims 19-21, 23, have been amended, claims 33-46 have been added, and claims 34-35, 39, 44 have been amended. Claims 19-46 are currently under prosecution.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC 112

4. Claims 20-25, 27-32, remain rejected under 35 USC 112, first paragraph and newly added claims 33-46 are rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed June 3, 2005, Section 4, pages 4-5.

Applicant argues that the rejection is grounded on the positions that the claims are drawn to an inferred anti-cancer vaccine and this position is improper. The argument has been considered but has not been found persuasive because contrary to Applicant's argument, the rejection is not grounded only in the inferred anti-cancer vaccine. In particular, the claims remained rejected at Section 5, pages 4-5 for the reasons previously set forth in the paper mailed August 25, 2004, Section 5, pages 5-18 wherein only a single section of that rejection was drawn to the inferred anti-cancer vaccine. Since Applicant responded only to the single section, Examiner's response to Applicant was also only drawn to that single section. Applicant's arguments were fully considered but not found persuasive and the rejection of record was maintained.

It is noted for Applicant's convenience that Examiner, in the interests of compact prosecution, examined the enablement of the claimed variant peptides and

polypeptides by (1) reviewing the known uses for SEQ ID NO:2. Since there is no known function for SEQ ID NO:2, it was made clear that there could not be a known function for the claimed variants of SEQ ID NO:2 based on homology to SEQ ID NO:2, especially in view of the teachings of Bowie, Burgess, Lazar, Scott, Bork and one would not know how to use the claimed variant invention (2) reviewing the predictability of antigen binding to antibodies produced from fragments of polypeptides and defining epitopes within polypeptides. Given the teachings of Roitt, Holmes et al, Herbert et al, Greenspan et al it is clear that the art is unpredictable and that one would not know how to use the claimed invention, (3) reviewing the predictability of T-cell recognition. Given the teachings of Kirken et al, Chaux et al, Sherman et al, Smith et al, it is clear that the art is unpredictable and that one would not know how to use the claimed invention. Since Applicant provided no arguments drawn to these grounds of rejection they were not addressed by Examiner and were maintained.

Applicant argues that one of the rejection's contentions has been shown to be factually in error wherein the specification specifically shows the putative glycosylation positions and discusses the glycosylation of the protein. The argument has been considered and has been found persuasive and the grounds of rejection drawn to lack of information drawn to glycosylation sites is hereby withdrawn.

Applicant argues that the statement that the specification contains no information on which epitopes are linear and which are conformational is set forth in relation to the improperly imported and non-existent vaccine recitations. The argument has been considered but has not been found persuasive for the reasons set forth above. Once again, although Applicant's previous arguments were drawn

only to the inferred vaccine limitations and Examiner's responses were drawn to Applicant's arguments, the rejections of the claims were not limited to the inferred limitations and still stand for the reasons of record.

Applicant argues that the Office has already issued a patent on antibodies to portions of SEQ ID NO:2. The argument has been considered but has not been found persuasive because the instant claims are not drawn to antibodies to portions of SEQ ID NO:2, but rather are drawn to variants of SEQ ID NO:2 and the claims are not enabled for the reasons previously set forth. The arguments have been considered but have not been found persuasive and the rejection is maintained.

5. Claims 20-25, 27-32, remain rejected under 35 USC 112, first paragraph and newly added claims 33-46 are rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed June 3, 2005, Section 6, pages 5-6.

Applicant argues that whether or not a given peptide is immunogenic and will induce the generation of antibodies against it is not generally considered to be a functional characteristic of a peptide or one that requires a disclosed correlation between function and structure and thus it appears that Examiner is importing claims to vaccine recitations into the claims. The argument has been considered but has not been found persuasive. Once again, although Applicant's previous arguments were drawn only to the inferred vaccine limitations and Examiner's responses were drawn to Applicant's arguments, the rejection of the claims in the action mailed August 25, 2004 did not even mention the inferred anti-cancer vaccine. Further, given the limitations of the claims as instantly constituted, drawn to use as an immunogen, recognition by T-cells, it is clear that in the absence of a correlation between structure and function, the specification does not provide a written description of the claimed invention. Further, if Examiner takes

Applicant's arguments on the face, it appears that Applicant is arguing that the claims do not include functional limitations and in the absence of functional limitations wherein those functions are related to a particular structure, it is clear that the specification does not provide a written description of the claimed variants.

Applicant argues that the written description requirement must be applied in the context of the particular invention and the state of knowledge in the art and points to *Capon v. Eshhar* wherein it was found that "when the prior art includes the nucleotide information, precedent does not set a per se rule that the information must be determined afresh". Further, Applicant reiterates arguments in the December 2004 Amendment drawn to *Lilly* and reiterates that the specification in *Lilly* contained no sequence information and that the present specification sets forth more than a mere wish or plan, it sets forth the entire amino acid sequence of mesothelin and refers to the raising of antibodies to subsequences of 10 or more amino acids of mesothelin which provides the information necessary for a practitioner to create subsequences of the protein and to raise antibodies to those peptides. Applicant further argues that what was known in the art was how to make peptides and how to raise antibodies to antigens and what was not known was the starting material, the sequence of mesothelin necessary to make these peptides.

The arguments have been considered but have not been found persuasive because Applicant has not demonstrated a nexus between the fact pattern in the instant specification and that in *Capon v. Eshhar*. In particular, although Applicant points to the ruling wherein if the sequence information is known in the prior art, it is unnecessary to provide it anew, although the specification provides SEQ ID NO:2, the sequences of the claimed variants are not in fact known. Given the

above, although Applicant suggests a similarity between the claims of the instant invention and the claims reviewed in the Eshhar case, Examiner fails to see any similarity between the two cases. In particular, unlike the known structure of the Eshhar claims, the structure of the broadly claimed variants is unknown because no structure function relationship has been identified for either the raising of antibodies which recognize full-length mesothelin or the recognition by T-cells from patients with mesothelioma- or ovarian cancer cells expressing mesothelin. Similar to the Lilly case, the broadly claimed, unknown structures are critical to the instant invention. Thus, the citation, by Examiner of Lilly is appropriate. Further, the Court, in *Capon v. Eshhar*, stated that it is appropriate to recognize the variability in the science in determining the scope of coverage to which the inventor is entitled and that the decision as to whether the claimed scope is appropriate usually focuses on the exemplification in the specification and the Court pointed specifically to Lilly and stated that the genus is not described where "a representative number of cDNAs defined by nucleotide sequence, falling within in the scope of the genus" had not been provided. Similar to the Lilly case, a representative number of variants which can be used as immunogens to raise antibodies which recognize full-length mesothelin, or are recognized by T-cells from patients with mesothelioma or ovarian cancer cells expressing mesothelin, except SEQ ID NO:2, falling within the scope of the genus has not been provided. The arguments have been considered but have not been found persuasive and the rejection is maintained.

6. Claims 20-25, 27-32, remain rejected under 35 USC 112, first paragraph and newly added claims 33-46 are rejected under 35 USC 112, first paragraph for the

reasons previously set forth in the paper mailed June 3, 2005, Section 8, pages 7-25.

Applicant argues that the instant rejection is not new, that the issues raised were adequately addressed in the December 2004 Amendment and Applicant reiterates said arguments. The argument has been considered but has not been found persuasive, the instant rejection was imposed in order to more clearly identify the issues and thus is in fact a new rejection.

Applicant argues that Examiner ignored Applicant's statements wherein certain statements in the references were not properly cited in the Office Action and states that Applicant's statements that the papers "did not seem to contain the statements attributed to them" was a respectful way of pointing out that the rejections appeared to be unsupported. Applicant further argues that Examiner's statement pointing to the fact that Applicant does not argue that the statements in the references are untrue is not proper examination practice. The argument has been considered but has not been found persuasive. Applicant in fact asked for "clarification". Thus, it was unclear to Examiner exactly what Applicant was requesting and given that no arguments drawn to the correctness of the statements were found, Examiner responded in what she felt was a proper manner. Examiner apologizes for any inconvenience from this misunderstanding.

Applicant argues that Bowie's teachings drawn to the critical nature of some residue substitutions does not show that there will be any effect on the immunogenicity of the protein. Applicant complains that Examiner ignores Applicant's statements that Bowie's statements are taken out of context and fails to consider Bowie's teachings as a whole and that Bowie's teaching supports the prediction that many substitutions can be made in SEQ ID NO;2 without affecting

the ability of the protein to generate antibodies or to bind T-cells activated by endogenous mesothelin. The argument has been considered but has not been found persuasive because Applicant is mischaracterizing Examiner's statements. Examiner clearly discusses the Bowie reference as it is drawn to the criticality of the unique three-dimensional structure and the nexus between that structure and the ability to raise antibodies. It is noted that Applicant neglects to discuss the teachings also set forth drawn to Herbert et al in that section of the rejection.

Applicant argues that Examiner misrepresents Applicant's arguments drawn to Boon. Applicant clarifies the point Applicant was making wherein if some cells of a tumor did not express the antigen, the patient would be benefited by killing or inhibition of those cells that do express the antigen and Applicant maintained that the alleged variability of antigen expression on cancer cells, even if true, did not affect the enablement of the invention. The argument has been considered but is found to be moot given that rejections drawn to inferred anti-cancer vaccine are withdrawn in the instant action.

Applicant argues that whether or not experimentation is undue is determined by the Wands factors and that although no experimentation is provided, the rejection is deficient because it does not address the other seven Wands factors. The argument has been considered but has not been found persuasive because Examiner clearly discusses the breadth of the variant claims, the nature of the invention, the state of the art, the level of one of ordinary skill, the level of predictability, the amount of guidance provided and the existence of working examples. Given this analysis, Examiner properly concluded that the quantity of experimentation required to make or use the invention based on the content of the

disclosure was undue. It is suggested that Applicant review the rejection set forth on pages 7-25 of Section 8 wherein each of these factors is clearly addressed.

Applicant argues that the level of skill in the art is high and that the amount of guidance needed is small and points to the Pastan Declaration. A review of the Pastan Declaration reveals that Dr. Pastan argues that it is a commonplace in the art that amino acid sequences of a protein determines its structure and that once a protein is expressed, epitopes on the protein can be mapped and these epitope maps identify the immunodominant portions of the protein, wherein individual peptides that raise antibodies can then be generated based on the portions of the molecule that are immunodominant and this work is considered to be routine in the art. The argument has been considered but has not been found persuasive because the claimed variants have not been expressed, the claims are not limited to fragments consisting of sequences of SEQ ID NO:2, the effects of undefined protein structure on the ability of those fragments to function as claimed can not be predicted for the reasons of record.

Applicant argues that only one utility is needed to enable an invention and loading dendritic cells with peptides was known in the art prior to the priority date of the application and this enables the claimed invention. The argument has been considered but has not been found persuasive because the argument is moot given that rejections drawn to the inferred anti-cancer vaccine are withdrawn in this action.

Applicant argues that Applicant has not mischaracterized the court's statements *In re Buchner* and states that the discussion in *Buchner* is relevant to the present claims. The argument has been considered but is moot considering that rejections drawn to the inferred anti-cancer vaccine are withdrawn in this action.

7. Claims 20, 23-25, remain rejected under 35 USC 112, first paragraph and newly added claims 34, 36, 38, 39-43 are rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed June 3, 2005, Section 9, pages 25-26.

Applicant argues that the text of the description of the specification makes it clear that the writer intended for the description of the first percentage of sequence identity carry to the others. The argument has been considered but has not been found persuasive because it is not possible for Examiner to determine the intentions of the writer. Examiner's analysis is limited to the text as originally filed and although Applicant states that "while perhaps not expressed with the precision that might be desired in hindsight" the text as originally filed does not support the newly added limitation and it is clear to Examiner that the limitation "at least" is not drawn to the 85% teaching.

Applicant further argues that the Action emphasizes the term "**has**" 85% identity" and that the phrase in the specification does not say that it has 85% identity as emphasized by the action but actually reads "or more preferably 85%". The argument has been considered but is not understood by Examiner. When Examiner emphasized the term "has" Examiner was merely pointing out an incorrect statement by Applicant. Applicant argues that MPEP 2163.05III instructs the Corps to take into account which ranges one of skill would consider inherently supported by the discussion in the original disclosure. The argument has been considered but has not been found persuasive as the teaching in the specification is not drawn to a range discussed in the MPEP wherein ranges are exemplified "described in the original specification included a range of "25%- 60%" and specific examples of "36%" and "50%." (see MPEP 2163.05III). The arguments

have been considered but have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC 102

8. Claims 19-32 remain rejected and claims 33-46 are rejected under 35 USC 102(b) for the reasons previously set forth in the paper mailed June 3, 2005, Section 7, pages 6-7.

Applicant argues that although the Action correctly recites the specification's definition of the terms "isolated", "purified' and "biologically pure", Applicant does not agree with the Action's findings that a protein identified in a Western blot is "substantially or essentially free from components which normally accompany it as found in its native state. Applicant reiterates previous arguments. The arguments have been considered but have not been found persuasive for the reasons previously set forth.

Further, in a telephone interview on February 28, 2006, given the definition of the term "recombinant" in the specification, Examiner felt that amending the claims to recite "recombinant" peptides could overcome the rejection of the Chang reference which is drawn to a protein isolated in a Western Blot. However, upon review and reconsideration it has become apparent that regardless of the method of making, that is recombinantly as defined in the specification or by isolation in a Western blot, the product claimed is in fact the same as that isolated in the Western blot. In particular, the production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when the properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re

Brown, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product per se, even when limited to the particular process, is unpatentable over the same product taught by the prior art. See In re Kind, 207 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); In re Merz, 97 F.2d 599, 601, 38 USPQ 143, 144-145 (CCPA 1938); In re Bergy, 563 F.2d 1031, 1035, 195 USPQ 344, 348 (CCPA 1977) *vacated* 438 U.S. 902 (1978); and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

Applicant points to page 8, line 30 to page 9 line 3 wherein the specification argues that it was not routine to clone the antigen and therefore the invention as claimed is unobvious over Chang. The argument has been considered but does not appear to be relevant to the instant rejection, given that the antigen of Chang meets the limitations of the instantly claimed inventions.

The arguments have been considered but have not been found persuasive and the rejection is maintained. Examiner apologizes for any inconvenience that addition consideration might cause.

New Grounds of Rejection

Claim Rejections - 35 USC 112

9. Claims 40-43 are rejected under 35 USC 112, second paragraph because the claims are drawn to "A composition of claim 35" and claim 36 does not recite a composition, rather claim 35 recites an "isolated polypeptide".

10. No claims allowed.

11. All other objections and rejections in the previous office action are hereby withdrawn.

12. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
May 5, 2006